

## Testimony for the October 2010 CFSAC Meeting by Jerrold Spinhirne

Several significant developments have occurred since the Committee met last May. The findings of the October 2009 *Science* paper by Lombardi et al. [1] of the Whittemore Peterson Institute, the National Cancer Institute, and the Cleveland Clinic have been confirmed by an FDA/NIH study by Lo et al. [2] published in August. Also, earlier in July, a CDC study by Switzer et al. [3] was unable to detect any retrovirus in CFS patient samples or in healthy controls. These events have important implications for the continuation of the CDC's CFS program and the work of the Committee.

The Lo et al. paper detected MLV-related retroviruses in 32 of 37 CFS patient samples, 86.5%, and in 3 of 44 control samples, 6.8%. This result agrees with the initial detection of XMRV, an MLV-related retrovirus, by Lombardi et al. in 68 of 101 CFS samples, 67.3%, and in 8 of 218 control samples, 3.7%. A subsequent paper by Mikovits et al. [4] published in July reports detecting XMRV in more than 75% of 101 CFS patient samples. This paper stresses the need to use multiple techniques to detect XMRV. Mikovits et al. also give likely reasons why two studies in the UK and one in the Netherlands failed to detect XMRV or related MLVs.

The CDC study by Switzer et al. is important because it raises the question of how the CFS program's established policies influence the results of its research. In the words of Dr. Suzanne Vernon, formerly of the CDC's CFS program, "This was a study designed to not detect XMRV using a hodge-podge sample set." [5] Patient samples were improperly handled and a method shown to be least sensitive was chosen to detect XMRV. The samples were collected from the subjects of three prior CDC studies who were determined to have CFS using the 2005 empiric criteria for CFS.

The empiric, or empirical, definition of CFS was described in a 2005 CDC paper. [6] The claim is made that use of three sets of questionnaires only operationalized, or standardized, the selection of CFS research subjects meeting the 1994 Fukuda definition. [7] In Switzer et al., the CFS subjects are described as meeting the International, or 1994 Fukuda, definition. However, this is not accurate. Research has shown that CFS cohorts selected using the empiric criteria are very different from CFS cohorts selected before 2005.

The adoption of the empiric criteria was a de facto redefinition of CFS by the CDC. The CDC's estimate for the prevalence rate for CFS jumped 10-fold using the empiric criteria – from 235 per 100,000 found in the CDC's 2003 Wichita study [8] to 2540 per 100,000 found in the CDC's 2007 Georgia study [9] Suddenly, 2.5% of the adult US population had chronic fatigue syndrome – if one discounts the CDC's speculation that this high rate of CFS might be a local Georgia phenomenon. Research on the CDC's empiric criteria has shown that it selects subjects having a higher rate of psychiatric co-morbidity and misdiagnoses 38% of patients having only major depressive disorder as having CFS. [10] The CDC's empiric definition lacks specificity, selecting subjects who do not meet the Fukuda criteria as

previously applied, and, surprisingly, also lacks sensitivity, missing subjects who do meet the Fukuda criteria. [11]

Of the 51 CFS subjects used in Switzer et al., it is likely that only about 10% actually could meet the 1994 Fukuda definition as it was applied in the CDC's 2003 study. [8] Given the .65 sensitivity of the empiric criteria [11], that would mean  $.65 \times 10\%$ , or less than 7% of the 51 CFS subjects actually would meet the Fukuda definition for CFS – 3 or 4 subjects. It is disingenuous for Switzer et al. to claim their CFS subjects met the 1994 International case definition for CFS.

**I request the Committee to reaffirm its October 2009 recommendation to the Department of Health and Human Services that the empiric criteria no longer be used in CFS research.** Research conducted using the empiric criteria, including Switzer et al., is not valid CFS research. Such research should only claim to be about the common symptom of fatigue, not CFS.

**I also request the Committee to recommend the 2003 Canadian Consensus Criteria be used for all CFS research and that researchers should work with experienced ME/CFS physicians to find subjects instead of using random telephone calls.** This year, Jason et al. [12] published a revision of the Canadian criteria specifically adapted for research purposes. Researchers outside of the CDC are already using this definition to insure consistent and meaningful results.

From the Discussion section of Switzer et al.:

“The Lombardi et al. study specifies that samples were selected from patients fulfilling the 1994 international CFS case definition and the 2003 Canadian Consensus Criteria for CFS/ME [sic]. Lombardi et al. did not specify if patients were evaluated for exclusionary conditions, or if the study subjects met both definitions, or which patients met either CFS definition.”

This is a curious comment. It appears the authors of Switzer et al. are questioning the meaning of the word “and.” They also imply that Lombardi et al. did not properly apply a research case definition, including its exclusions.

“The 1994 International CFS case definition and the Canadian Consensus Criteria are different and do not necessarily identify similar groups of ill persons. Most notably, the Canadian Criteria include multiple abnormal physical findings such as spatial instability, ataxia, muscle weakness and fasciculation, restless leg syndrome, and tender lymphadenopathy. The physical findings in persons meeting the Canadian definition may signal the presence of a neurologic condition considered exclusionary for CFS and thus the XMRV positive persons in the Lombardi et al. study may represent a clinical subset of patients.”

Again, the authors seem not to recognize that all of the Lombardi et al. CFS subjects met the CDC's 1994 International definition. This is a particularly awkward comment from the

authors of a study in which over 90% of the CFS subjects did not meet the International definition as claimed. The authors also seem to want both to exclude Canadian criteria subjects from CFS and include them as a subset of CFS – a logical impossibility. The “neurologic condition” they wish to exclude from CFS has no diagnosis in the US other than CFS.

For 25 years, it has been the unstated policy of the CDC to marginalize CFS as an unimportant psychogenic illness rather than acknowledge what it is – a serious neuro-immune disease. Whenever evidence was found of immunological or neurological abnormalities or association with pathogens, the CDC has dismissed the evidence and/or claimed the patients being studied have something other than CFS. In 1992, Buchwald et al. published a study "A Chronic Illness Characterized by Fatigue, Neurologic and Immunologic Disorders, and Active Human Herpesvirus Type 6 Infection." [13] Reeves et al. of the CDC responded with a comment letter [14] ending, "We conclude that the disease Buchwald and co-workers described is not chronic fatigue syndrome or any other clinical entity, and that they showed no association with active HHV-6 replication." The same denial is true for literally thousands of other peer-reviewed research papers.

The effect of this policy has been to deny appropriate medical care and assistance to hundreds of thousands of severely ill and disabled people in the US. The enormity of the harm and suffering caused by the CDC's CFS policy makes it difficult to comprehend. It is shameful that the CDC has betrayed its mission and the public trust by allowing its CFS program to block outside research and progress in understanding the disease.

In September 1985, a quarter century ago, the CDC sent two inexperienced investigators to Incline Village, Nevada in response to repeated requests for assistance concerning the outbreak of a mysterious illness. The CDC failed to recognize the similarities of this illness to myalgic encephalomyelitis, which had been studied since the 1950s and recognized as a neurological disease by the World Health Organization in 1969. Instead, with the 1988 Holmes definition they created a new disorder and gave it the trivializing name chronic fatigue syndrome, based on the misconception that fatigue is a defining feature. Fatigue is subjective and is a commonly reported symptom of many physical illnesses and psychiatric disorders.

The CDC broadened its criteria for selecting CFS research subjects with the Fukuda definition [7] in 1994. The only required symptom is fatigue for 6 months. The other symptoms are optional, if 4 of 8 listed symptoms are present. The hallmark symptoms of post-exertional malaise and cognitive impairment need not be present. The Fukuda definitional paper also specifically recommended that no testing be performed in clinical settings to help doctors diagnose and treat CFS.

"The use of tests to diagnose the chronic fatigue syndrome (rather than to exclude other diagnostic possibilities) should be done only in the setting of protocol-based research. The fact that such tests are investigational and do not aid in diagnosis or management should be explained to the patient."

The very tests for immune dysfunction and pathogens that had been found to be associated with CFS by non-CDC researchers were listed as tests not to be performed. This list of medical tests and imaging studies not to be done for CFS patients is still on the CDC's CFS website to this day under "Theoretical and Experimental Tests" having "no demonstrated value." [15] Only routine tests to exclude other diagnoses are recommended by the CDC.

**I request the Committee to recommend that the tests the CDC considers theoretical and experimental be independently evaluated for their appropriateness in helping doctors to diagnose CFS.**

Use of the empiric criteria for CFS research enabled the CDC to collaborate with Emory University's department of psychiatry and their mind-body program to produce a series of papers purporting to show links between adverse childhood events or abuse and CFS. [16, 17] The latest in this series, published in July 2010, claims that patients with CFS have an association with "an increased prevalence of maladaptive personality features and personality disorders. This might be associated with being noncompliant with treatment suggestions, displaying unhealthy behavioral strategies and lacking a stable social environment." [18] This research on alleged CFS amounts to little more than defamation of severely ill and disabled people. It is shameful that the CDC participated in this study and made it possible by failing to adequately define CFS for 25 years.

**A dramatic increase in research funding is now needed to study the pathogenesis and transmission of XMRV and other MLV-related retroviruses in CFS. Early clinical trials are essential.** However, as an ME/CFS patient who has been unable to work or participate in life for 14 years, I would like to see this funding go only to research organizations which place science above policy.

Thank you for this opportunity to submit my testimony and your work on our behalf.

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